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TITLE: Method for detection of specific target cells in specialized or mixed cell population and solutions containing mixed cell populations

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INVENTOR-INFORMATION:

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CLAIMS:

We claim:

1. A method for detecting and quantitating a specific living target cell in a cell suspension of a mixed cell population at a sensitivity of one target cell per 100 or more total cells, in a fluid system containing a mixed cell population, or in a single-cell suspension prepared from a solid tissue, with the exception of normal and malignant hematopoietic cells in blood and bone marrow, the method comprising the steps of:

a. coating paramagnetic particles or beads with an antibody or antibody fragment directed against a membrane structure specifically expressed on the target-cell and not on a non-target-cell in the cell mixture;

b. mixing the coated paramagnetic particles or beads with the cell suspension containing the target-cells;

c. incubating the mixture under gentle rotation;

d. examining the target-cells after incubation; and

e. counting the target-cells after incubation.

2. The method of claim 1, wherein the paramagnetic particle or bead is coated with a murine or a human antibody or fragment thereof.

3. The method of claim 1, wherein incubating lasts for 5-10 minutes to 2 hours.

4. The method of claim 3, wherein incubating lasts 30 minutes.

5. The method of claim 1, wherein incubating is at a temperature between 0.degree. C. and 25.degree. C.

6. The method of claim 5, wherein incubating is at a temperature of about 4.degree. C.

7. The method of claim 1, wherein when the target cell population is contained in blood or bone marrow aspirates, the method further comprises the step of:

pre-incubating the antibody-coated paramagnetic particle and the cell suspension with mild detergent.

8. The method of claim 7, wherein the preincubating comprises as detergent Tween 20.TM. (polyoxyethylenesorbitan monolaurate) at a concentration less than 0.1% and the preincubation lasts 30 minutes at 4.degree. C.

9. The method of claim 1, wherein when the density of target-cells is low, or when the ratio of target cell/total cells in the cell mixture is low (.ltoreq.1%), the method further comprises the step of:

subjecting the incubated paramagnetic particle-antibody-cell mixture to a magnetic field.

10. The method of claim 9, wherein the particle-target-cell complexes are stained.

11. The method of claim 1, wherein the step of examining, the step of counting, or both steps comprise using a microscope or a cell or particle counting device.

12. The method of claim 1, further comprising the steps of:

isolating the target-cells by exposing the complex of cells and paramagnetic particles to a magnetic field to magnetically aggregate the cells;

subjecting the magnetically aggregated cells to further biological, biochemical, and immunological examination.

13. The method of claim 1, wherein the antibody or fragment thereof is directed against an antigen or a receptor in a cell with abnormal developmental patterns.

14. The method of claim 13, wherein the cell is a primary or a metastatic cancer cell.

15. The method of claim 13, wherein the antibody or antibody fragment is directed against breast, ovarian or lung carcinoma cells; melanoma, sarcoma, glioblastoma or cancer cells of the gastrointestinal tract; melanoma, sarcoma, glioblastoma or cancer cells of the genitourinary tract; or melanoma, sarcoma, glioblastoma or cancer cells of the reticuloendothelial system.

16. The method of claim 1, wherein the antibody or fragment is of IgG isotype, a F(ab').sub.2 fragment, a F(ab) fragment, IgM, or a fragment of IgM.

17. The method of claim 1, wherein the cell suspension or population comprises mammalian tissue, a pleural effusion, a peritoneal effusion, a body fluid, or a solid tumor in a normal tissue or organ.

18. The method of claim 17, wherein the mammalian tissue comprises human bone marrow or human peripheral blood; the body fluid comprises urine, cerebrospinal fluid, semen, or lymph; or the normal tissue or organ comprises liver, lymph node, spleen, lung, pancreas, bone, central nervous system, prostate gland, skin, or mucous membranes.

19. A kit for performing the method of claim 1, the kit comprising:

a. a specific antibody or antibody fragment directed to an antigen on a target-cell, which antibody or fragment is effective for coating a paramagnetic particle or bead without removing its antigen-binding ability;

b. a paramagnetic particle or bead; and

c. another specific antibody or antibody fragment directed against an antigen or a receptor within or on the target cell;

wherein said another antibody or antibody fragment is conjugated to biotin or to an enzyme; or wherein said another antibody or antibody fragment is bound to a non-paramagnetic particle with a specific color or with a bound enzyme.

20. The kit of claim 19, wherein the enzyme is peroxidase or alkaline phosphatase.

21. A method for detecting a specific living target cell in a cell suspension of a mixed cell population at a sensitivity of one target cell per 100 or more total cells, in a fluid system containing a mixed cell population, or in a single cell suspension prepared from a solid tissue, with the exception of normal and malignant hematopoietic cells in blood and bone marrow, the method comprising the steps of:

a. coating paramagnetic particles or beads with an antibody or antibody fragment directed against a membrane structure specifically expressed on the target-cell and not on a non-target-cell in the cell mixture;

b. mixing the coated paramagnetic particles or beads with the cell suspension containing the target-cells;

c. incubating the mixture under gentle rotation; and

d. examining the target-cells after incubation.